



1 / 32

CTCGAGGACAGTGACCTGGGAGTGAGTACAAGGTGAGGCCACCACTCAGGGT  
GCCAGCTCCAAGCGGGTCACAGGGACGAGGGCTGCGGCCATCAGGAGGCCCT  
GCACACACATCTGGGACACGCGCCCCCGAGGGCCAGTTCACCTCAGTGCGCC  
TCATTCTCCTGCACAAAAGCGCCCCCATCCTTTCTTCACAAGGCTTTCGTGG  
AAGCAGAGGCGTCGATGCCCAGTACCCTCTCCCTTTCCCAGGCAACGGGACC  
CCAAGTTTGCTGACTGGGACCACCAAGCCACGCATGCGTCAAGAGTGAGAGT  
CCGGGACCTAGGCAGGGGCCCTGGGGTTGGGCCTGAGAGAGAAGAGAACCTC  
CCCCAGCACTCGGTGTGCATCGGTAGTGAAGGAGCCTCACCTGACCCCCGCT  
GTTGCTCAATCGACTTCCCAAGAACAGAGAGAAAAGGGAACCTTCAGGGCGG  
CCCGGGCCTCCTGGGGGTTCCCAACCCCATTTTTAGCTGAAAGCACTGAGGCA  
GAGCTCCCCCTACCCAGGCTCCACTGCCCGGCACAGAAATAACAACCACGGT  
TACTGATCATCTGGGAGCTGTCCAGGAATTC

## FIG.\_1A

1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC  
51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT  
101 GAGCTAGGCT AACTGGGTT TGGCTGGGCT GGGCTGGGCT GGG

## FIG.\_2B

1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTCAGCTG AGCGGGTTGG  
51 GTTAGACTGG GTCAAAGTGG TTCAGC

## FIG.\_2C

BEST AVAILABLE COPY

# GERMLINE & LOCUS

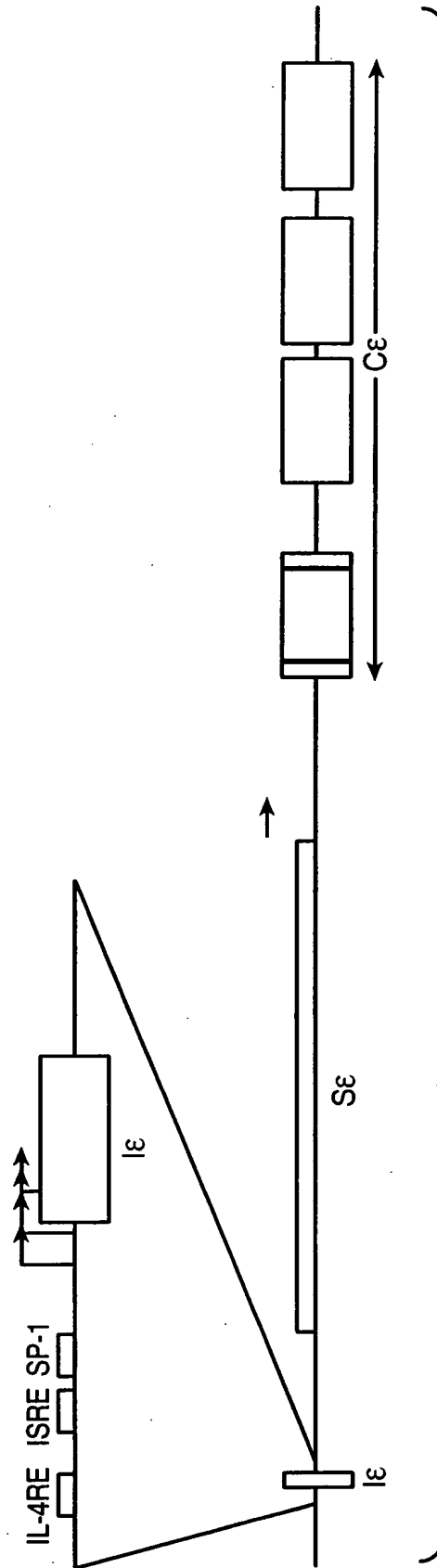
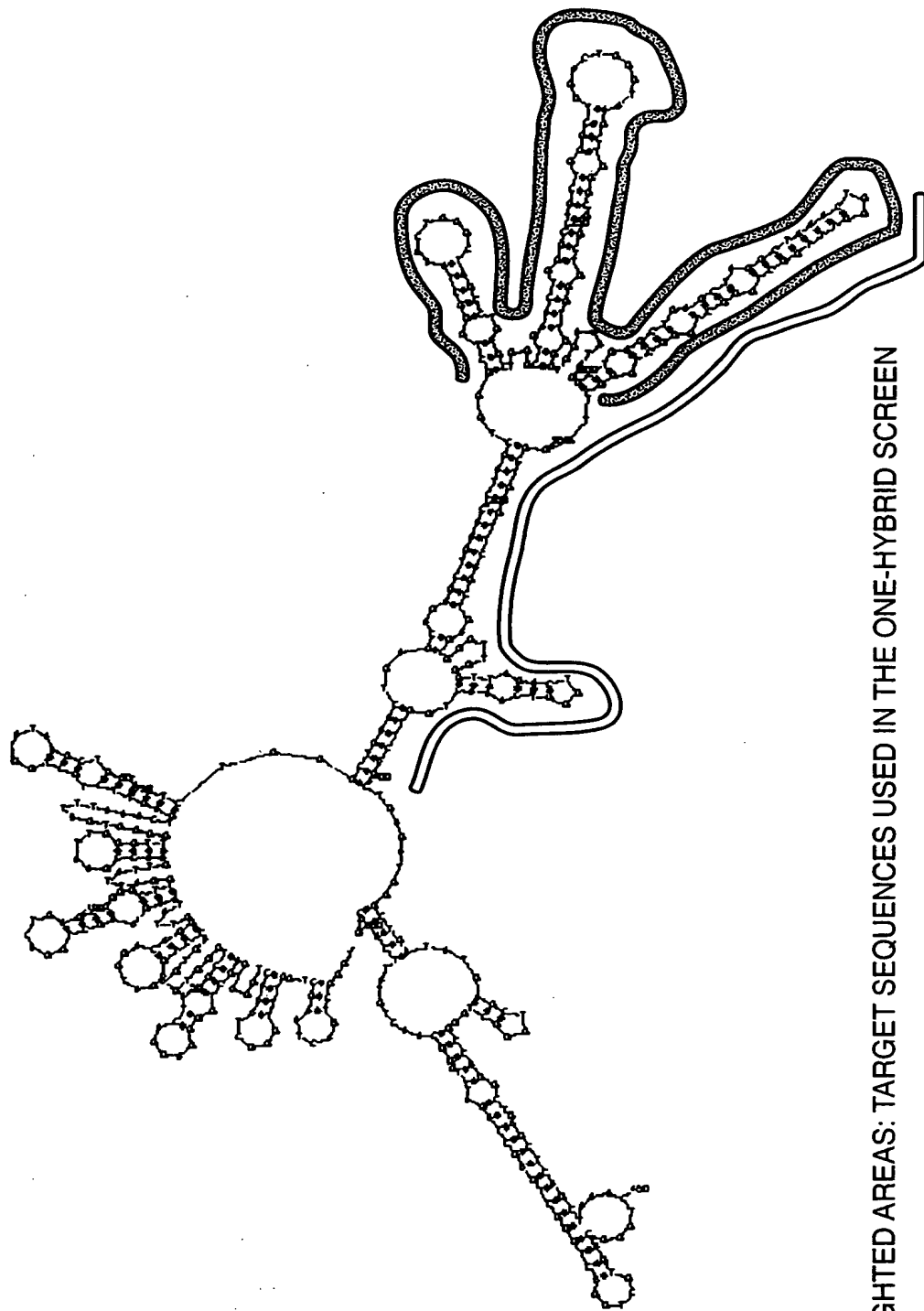


FIG. 1B

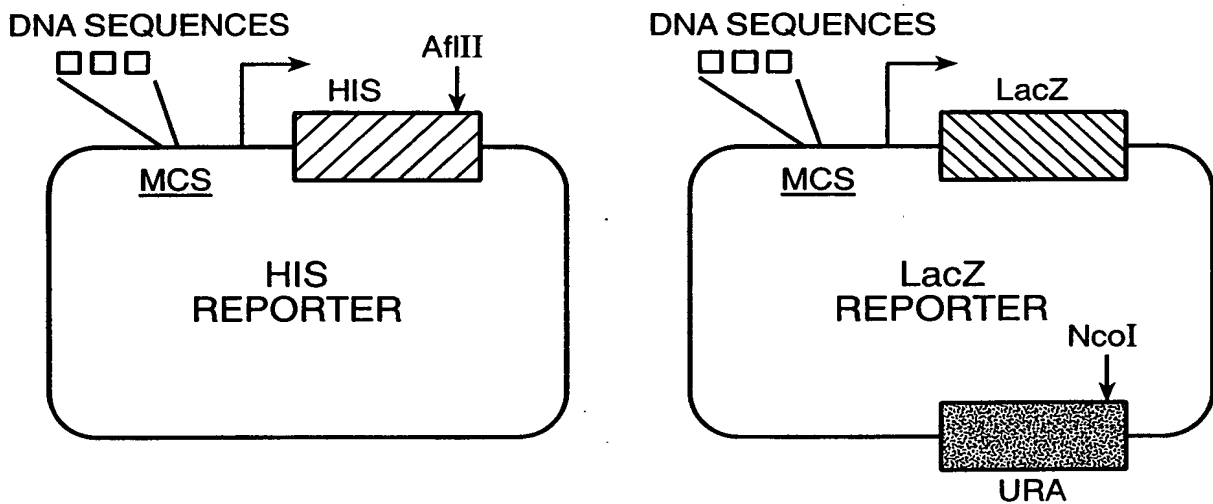
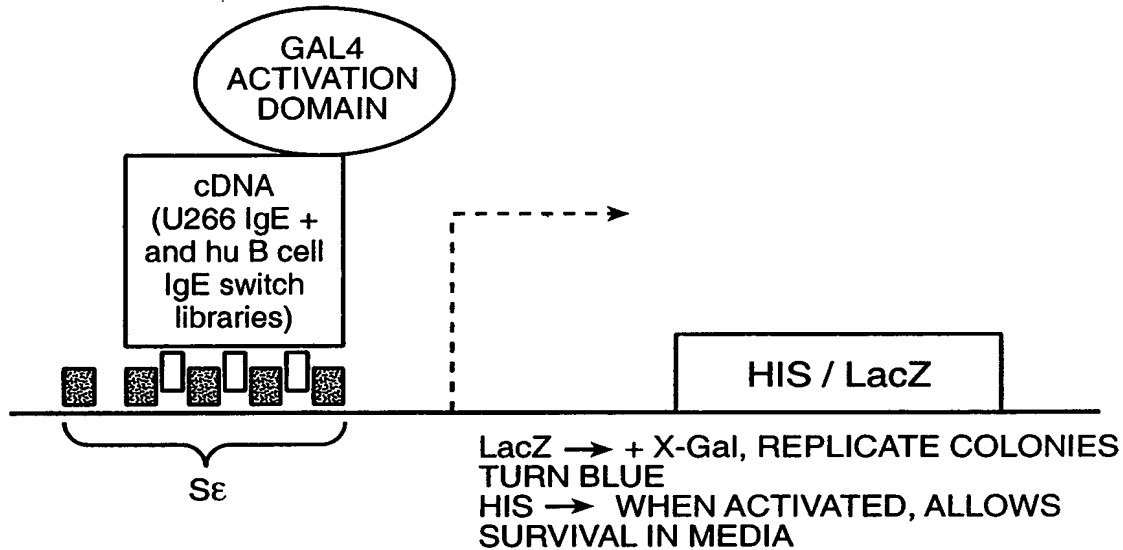
LOW ENERGY DNA FOLDING OF THE S $\epsilon$  REGION



HIGHLIGHTED AREAS: TARGET SEQUENCES USED IN THE ONE-HYBRID SCREEN

**FIG..2A**

## YEAST ONE-HYBRID SCREENING



ONE HYBRID REPORTER VECTORS  
DNA SEQUENCES OF INTEREST ARE INSERTED INTO THE MULTIPLE  
CLONING SITES (MCS). THE ENZYME USED TO LINEARIZE THE  
VECTOR IS SHOWN WITH A SOLID ARROW. DASHED ARROWS  
INDICATE THE TRANSCRIPTION OF THE REPORTER GENE.

**FIG. 3**

DND39 + IL-4

DND39 - IL-4

MC-116 + IL-4

MC-116 - IL-4

CA-46 + IL-4

CA-46 - IL-4

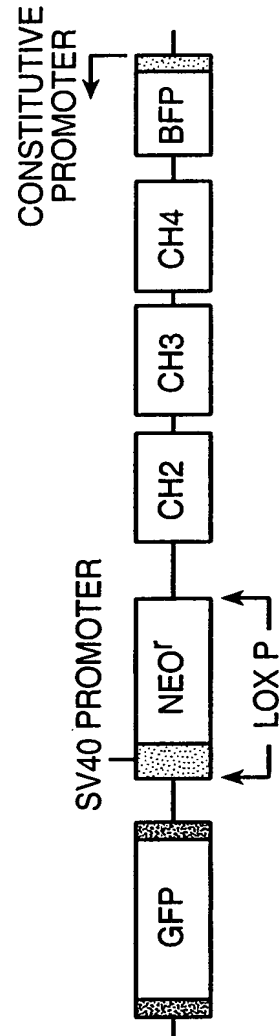
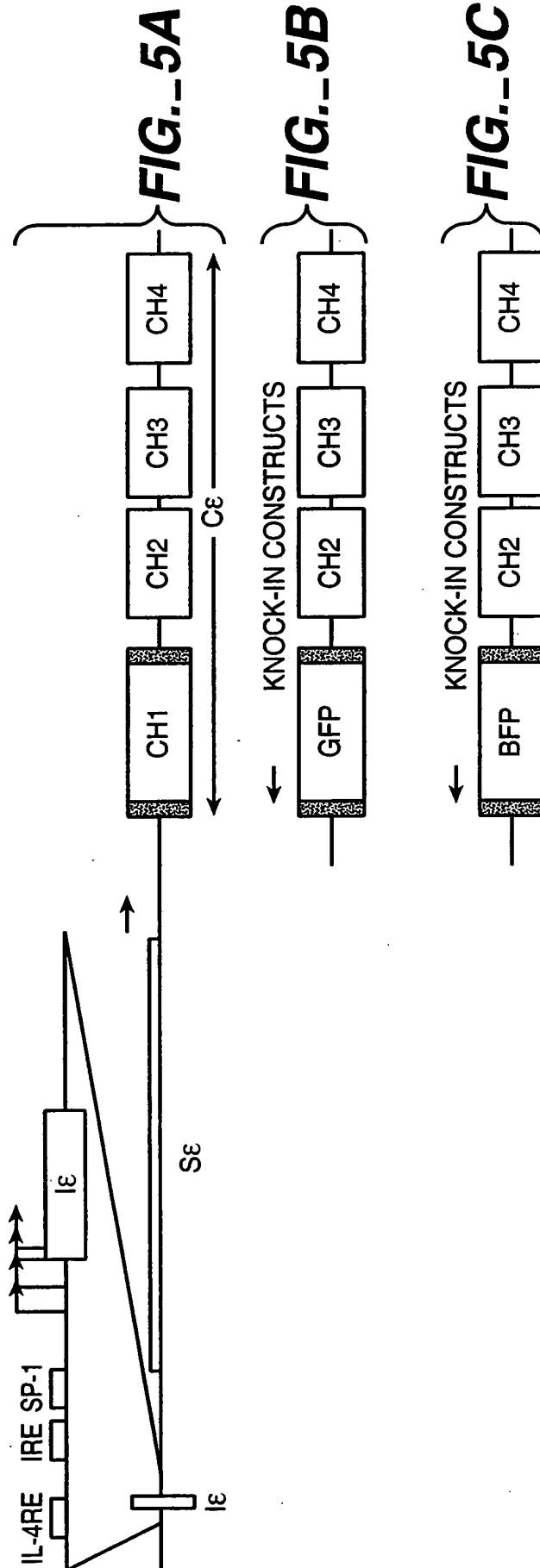
NEG. CONT.



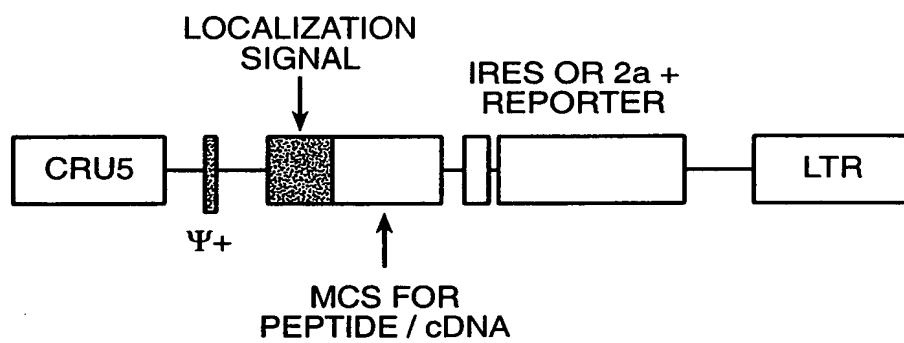
**FIG.\_4**

246bp

123 bp



IL-4 RE, IL-4 RESPONSIVE ELEMENT  
IRE, INTERFERON RESPONSIVE ELEMENT  
SP-1, SP-1 BINDING SITE  
I $\epsilon$ , NON-TRANSLATED EXON  
S $\epsilon$ , SWITCH REGION OF  $\epsilon$   
GFP, GREEN FLUORESCENT PROTEIN  
BFP, BLUE FLUORESCENT PROTEIN  
CH1,2,3,4, CONSTANT REGION DOMAIN EXONS



**FIG.\_6**

# PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS AND INFECTION OF NONADHERENT TARGET CELLS

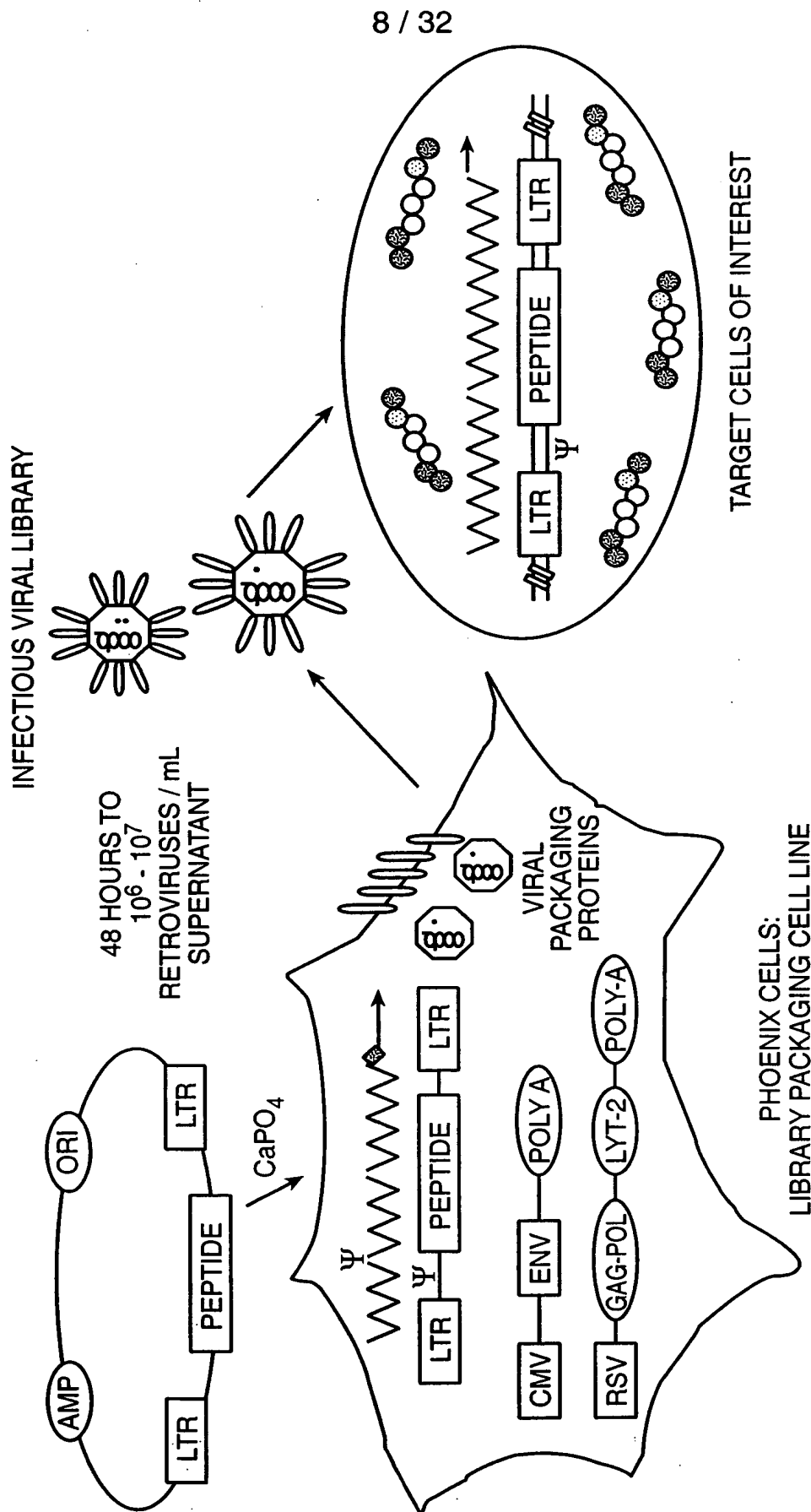
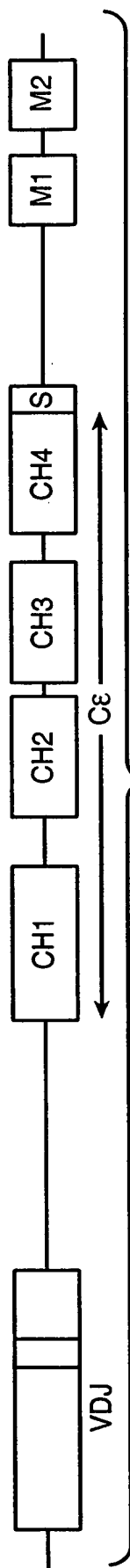


FIG. 7



# ε HEAVY CHAIN GFP / BFP KNOCK-IN CELL LINE

U266 ε HEAVY CHAIN

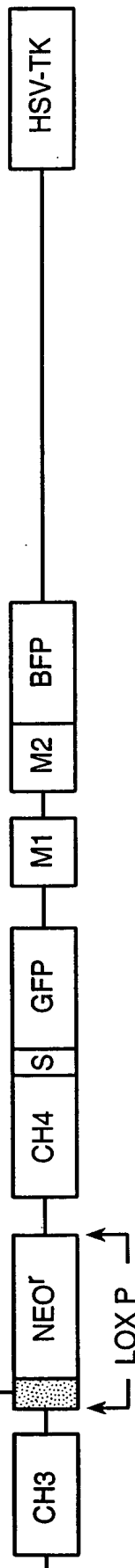


**FIG.\_8A**

9 / 32

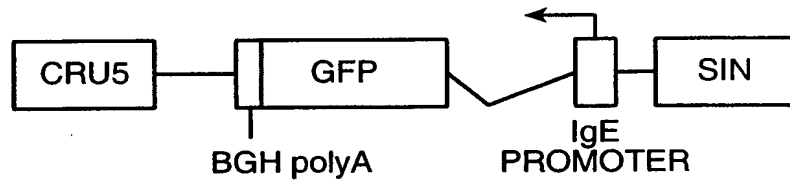
KNOCK-IN CONSTRUCT

SV40 PROMOTER

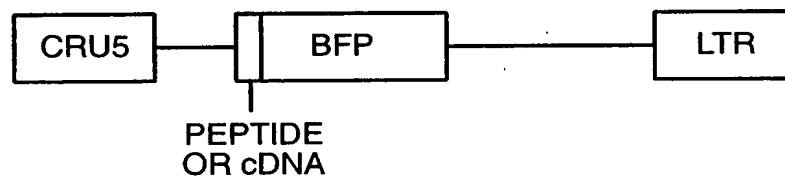


U266 CELLS ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE TREATED WITH GANCICLOVIR (HSV-TK DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH *cre* TO REMOVE THE SV40 NEOMYCIN RESISTANCE GENE.

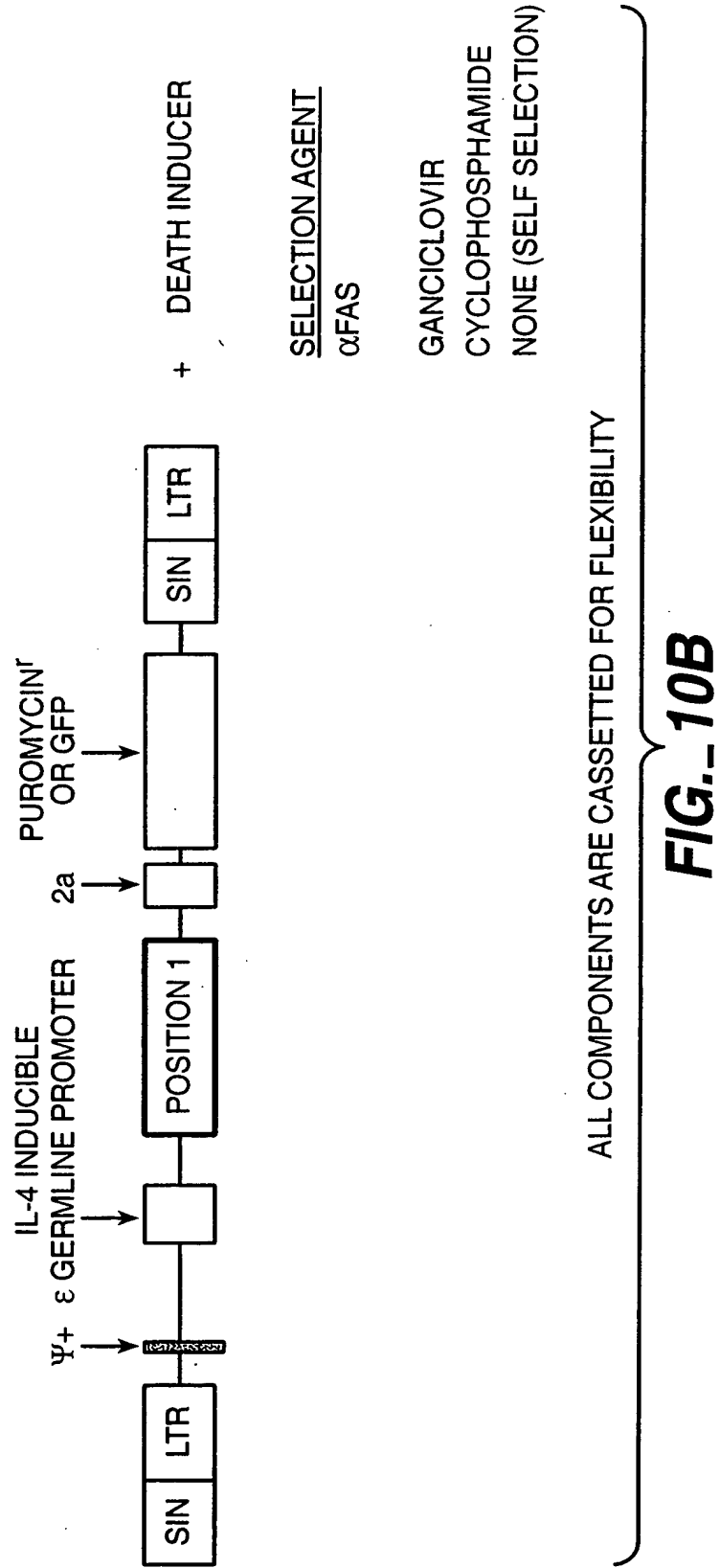
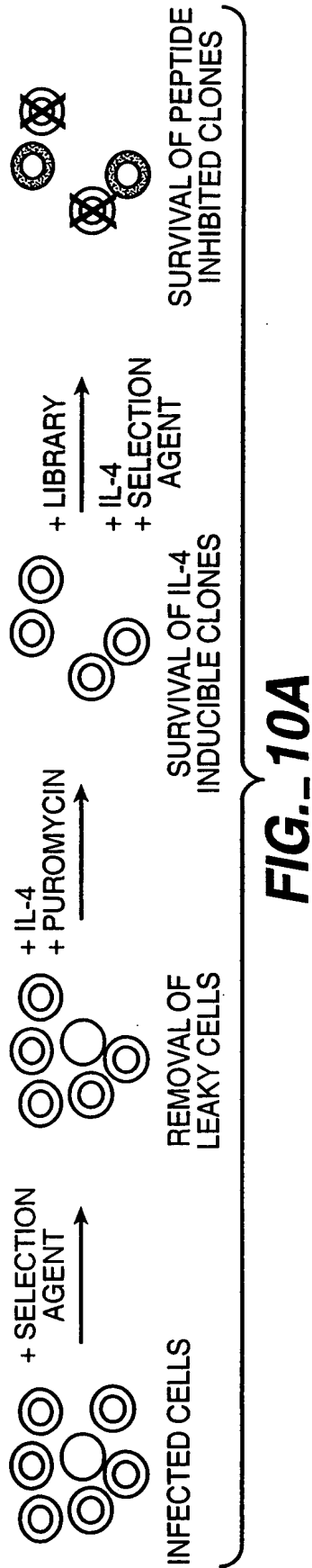
**FIG.\_8B**



**FIG.\_9A**



**FIG.\_9B**



ALL COMPONENTS ARE CASSETTED FOR FLEXIBILITY

1-845 CMV promoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended  $\Psi$  region  
 2146-2173 two Bstx1 peptide cloning sites  
 2205-2723 ECMV IRES (cloned as EcoR1/MscI fragment from  
     pCITE-4a [Novagen])  
 2746-3465 GFP coding region  
 3522-4115 3' LTR  
 4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC  
 CAAACTCAAATATATAAAGCATTTGACTTGTCTATGCCCTAGTTATTAATAGTAATCAA  
 TTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA  
 ATGGCCCGCCTGGCTGACCGCCCAACGACCCCGCCCATTTGACGTCAATAATGACGTATG  
 TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT  
 AAAGTGGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG  
 TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC  
 CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC  
 AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA  
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 GAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGACAGTTGCATCCGACTTGTGGT  
 CTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT  
 CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACACCGACCCACCACCG  
 GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA  
 TTTTATGCGCCTGCGTCCGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG  
 TGGAAGTACGAGTTTCGGAACACCCGGCCGCAACCCCTGGGAGACGTCCCAGGGACTTCGG  
 GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTTGGACTCTTTGGTG  
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 CGCCTCCGTCTGAATTTTTGCTTTTCGGTTTGGGACCGAAGCCGCGCCGCGCTCTTGTCT  
 GCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAATA  
 TCGGCCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACCTGGAAGATG  
 TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTACCTTCT  
 GCTCTGCAGAAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG  
 ACCTCATCACCCAGGTAAAGATCAAGGTCTTTTACCTGGCCCGCATGGACACCCAGACC  
 AGGTCCCCCTACATCGTGACCTGGGAAGCCTTGGCTTTTGACCCCCCTCCCTGGGTCAAGC  
 CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCTCCATCCGCCCCGTCTCTCCCCCTTG  
 AACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG  
 GCGCCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCGCCCTTGTAACCTTCC  
 CTGACCCTGACATGACAAGAGTTACTAACAGCCCCCTCTCTCCAAGCTCACTTACAGGCTC  
 TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACCTGG  
 ACCGACCGGTGGTACCTCACCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC  
 AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCTTGCTGACCACCCCA  
 CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCACGTGAAGGCTGCCGA  
 CCGGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC  
 CCATTAAATTGGAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGCGAATTAATTCC

GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG  
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CCTACGGCGTGACGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGCACTTCTTCA  
AGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCA  
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ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAAGCGGCATCAAGGTGAAC  
TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGACGCTCGCCGACCCTACCAGCAGA  
ACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCAGT  
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CCGCCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA  
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GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGA  
GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA  
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CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTTC  
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CACTGACTCGCTGCGCTCGGTCTGCTCGGCGAGCGGTATCAGTCACTCAAAGGC  
GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG  
CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG  
CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG  
ACTATAAAGATACCAGGCGTTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC  
CCTGCCGCTTACCGGATACCTGTCCGCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA  
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CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG  
AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC

TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT  
TGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGGTTTGCAA  
GCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGG  
GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA  
AAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAATCTAAAG  
TATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC  
AGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC  
GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC  
ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGG  
TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG  
TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTC  
ACGCTCGTCGTTTGGTATGGCTTCATTACGCTCCGGTTCCTCAACGATCAAGGCGAGTTAC  
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AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC  
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GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT  
CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG  
ATCTTCAGCATCTTTTACTTTACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA  
TGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTT  
TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG  
TATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTT

*FIG.\_11A-3*

1-845 CMVpormoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended  $\square$  region  
 2151-2865 GFP coding region  
 2866-2894 GGGSGGG linker  
 2895-2952 FMDV 2a cleavage sequence  
 2953-3004 Bstx1/Bstx1/Hind3/Hpa1/Sal1/Not1 polylinker  
 3052-3645 3' LTR  
 3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC  
 CCAAACCTCAAATATATAAAGCATTGTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC  
 AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCGCGTTACATAAATTACGG  
 TAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCATTGACGTCAATAATGACG  
 TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT  
 ACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA  
 TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGG  
 GACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG  
 GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTC  
 TCCACCCCATTTGACGTCAATGGGAGTTTGT TTTGGCACCAAAATCAACGGGACTTTCCA  
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 GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCAACCCCTCACTCGGGGCGCCAGTC  
 CTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCAAGTTGCA  
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 ACGTCCCAGGGACTTCGGGGGCGGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT  
 CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA  
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 GACCTTAGGTCACCTGGAAAGATGTGCGAGCGGATCGCTCACAAACAGTCGGTAGATGTCA  
 AGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAAATGGCCAACCTTTAACGTCGGATGG  
 CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC  
 ACCTGGCCCCGCATGGACACCCAGACCAGGTCCCCCTACATCGTGACCTGGGAAGCCTTGG  
 CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTT  
 CCTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTC  
 CCTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTAT  
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 AGCCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG  
 ACCTCTGGCGGCAGCCTACCAAGAACAACCTGGACCGACCGGTGGTACCTCACCCCTTACC  
 GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG  
 AAAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGC  
 AGCTTGGATACACGCCGCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA  
 GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCCGGG

FIG. 11B-1

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTC  
 CGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA  
 CCGGCAAGCTGCCCGTGCCCTGGCCCCACCTCGTGACCACCTGACCTACGGCGTGCGAG  
 TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCAGACTTCTTCAAGTCCGCCATGCC  
 CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC  
 GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC  
 GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACATAACAGCCA  
 CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACCTCAAGATCC  
 GCCACAACATCGAGGACGGCAGCGTGCGAGCTCGCCGACCACTACCAGCAGAACACCCCC  
 ATCGGCGACGGCCCCGTGCTGCTGCCCCGACAACCACTACCTGAGCACCCAGTCCGCCCT  
 GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCTTGCTGGAGTTCGTGACCGCCG  
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 GGTGAGCTGTTGAATTTTGACCTTCTTAAACTTGCGGGAGACGTCGAGTCCAACCTGG  
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 GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA  
 CTGAGAAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAAACAGCTGAATATGGGCC  
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 AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTTCCCCCTGGAAGCTCCCT  
 CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCTTTCTCCCTT  
 CGGGAAGCGTGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC  
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 CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG  
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 TTAAGGGATTTTGGTTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT  
 AAAAAATGAAGTTTGCAGCAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT  
 TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCAT  
 AGTTGCCTGACTCCCCGTGCTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCC  
 CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA

FIG. 11B-2



AACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCAT  
CCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC  
GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCGTTTGGTATGGCT  
TCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAA  
AAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGT  
TATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGA  
TGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAAATAGTGTATGCGGCG  
ACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGCGCCACATAGCAGAACTT  
TAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCG  
CTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTT  
TACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGG  
GAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTTCAATATTATTGA  
AGCATTTATCAGGGTTATTGTCTCATGACATTAACCTATAAAAATAGGCGT

**FIG.\_11B-3**

1-845 CMVpormoter/R/U5 5' LTR  
 1322 GAG ATG-ATC mutation  
 850-2100 extended - region  
 2146-2173 two Bstx1 peptide cloning sites  
 2173-2214 Eor1/Apa1/Hpa1/Not1 polylinker  
 2262-2855 3' LTR  
 2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC  
 CCAAACCTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC  
 AATTACGGGGTCATTAGTTCATAGCCATATATGGAGTTCCGCGTTACATAAATTACGGT  
 AAATGGCCCCGCTGGCTGACCGCCCAACGACCCCCGCCCATTTGACGTCAATAATGACGT  
 ATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTA  
 CGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTAT  
 TGACGTCAATGACGGTAAATGGCCCCGCTGGCATTATGCCCAGTACATGACCTTATGGG  
 ACTTTCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGG  
 TTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCGAAGTCT  
 CCACCCCATTTGACGTCAATGGGAGTTTGTGTTTGGCACCAAAATCAACGGGACTTTCCAA  
 AATGTCGTAACAACCTCCGCCCCATTGACGCAAAATGGGCGGTAGGCATGTACGGTGGGAG  
 GTCTATATAAGCAGAGCTCAATAAAAGAGCCACAAACCCCTCACTCGGGGCGCCAGTCC  
 TCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCAAGTTGCAT  
 CCGACTTGTGGTCTCGCTGTTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTC  
 AGCGGGGGTCTTTTCAATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCA  
 CCGACCCACCACCGGGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCT  
 AGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTA  
 TCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCCTGGGAGA  
 CGTCCCAGGGACTTCGGGGGCGCGTTTGTGTCGCCCGACCTGAGTCCAAAAATCCCGATC  
 GTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGGATATGTGGTTCTGGTAGGAGAC  
 GAGAACCTAAAAACAGTTCCCGCCTCCGTCTGAATTTTGTCTTTCCGGTTTGGGACCGAAG  
 CCGCGCCGCGCGTCTTGTCTGCTGCAGCATCGTTCTGTGTTGTCTCTGTCTGACTGTGT  
 TTCTGTATTTGTCTGAAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTG  
 ACCTTAGGTCACCTGGAAAGATGTGCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAA  
 GAAGAGACGTTGGGTACCTTCTGCTCTGCAGAAATGGCCAACCTTTAACGTCGGATGGC  
 CGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCA  
 CCTGGCCCCGATGGACACCCAGACAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGC  
 TTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTTC  
 CTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTTCGACCCCGCCTCGATCCTCC  
 CTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATA  
 TGGGGCACCCCCGCCCCCTTGTAACCTTCCCTGACCCCTGACATGACAAGAGTTACTAACA  
 GCCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGA  
 CCTCTGGCGGCAGCCTACCAAGAACTGAGACCGACCGGTGGTACCTCACCCCTTACCG  
 AGTCGGCGACACAGTGTGGGTCCGCGGACACCAGACTAAGAACCTAGAACCTCGCTGGA  
 AAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGCA  
 GCTTGGATACACGCCGCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAG  
 ACTGCCGGATCTCGAGGGATCCACCACCATGGACCCCATTAATTTGGAATTCGGGGCC  
 CAAGCTTTGTTAACGTCGACGCGGCCGCGCTCGACGATAAAATAAAAGATTTTATTTAG  
 TCTCCAGAAAAAGGGGGGAATGAAAGACCCACCTGTAGGTTTGGCAAGCTAGCTTAAG  
 TAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAG  
 TTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGA  
 TATCTGTGGTAAGCAGTTTCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG  
 CGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA  
 CCTGAAATGACCTGTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTCGCTTCTGTT  
 CGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCC  
 AGTCCTCCGATTGACTGAGTCGCCCCGGGTACCCGTGTATCCAATAAACCCCTCTTGCACT  
 TGCATCCGACTTGTGGTCTCGCTGTTCTTGGGAGGGTCTCCTCTGAGTGATTGACTAC  
 CCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCT  
 CTGAGTGATTGACTACCCGTCAGCGGGGGTCTTACATGCAGCATGTATCAAAATTAAT  
 TTGGTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC  
 AACGCGCGGGGAGAGGGCGGTTTGCCTATTGGCGCTCTTCCGCTTCTCGCTCACTGACT  
 CGCTGCGCTCGGTCTGTTCCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATA  
 CGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCA  
 AAAGGCCAGGAACCGTAAAAAGGCCGCGTGTGGCGTTTTTCCATAGGCTCCGCCCCC  
 CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA  
 TAAAGATACCAGGCGTTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT  
 GCCGCTTACCAGGATACCTGTCCGCTTTCTCCCTTCGGGAAGCGTGCGCTTTTCTCATA  
 GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTGCTTCGCTCCAAGCTGGGCTGTGTG  
 CACGAACCCCCCGTTTCAGCCCCGACCGCTGCGCCTTATCCGGTAACCTATCGTCTTGAGTC  
 CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCA  
 GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC  
 ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAG  
 AGTTGGTAGCTCTTGATCCGGCAAACAAACACCGCTGGTAGCGGTGGTTTTTTTTGTTT  
 GCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCT  
 ACGGGGTCTGACGCTCAGTGGAACGAAACTCACGTTAAGGGATTTTGGTCATGAGATT  
 ATCAAAAAGGATCTTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAA  
 TCTAAAGTATATATGAGTAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA  
 CCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA  
 GATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAG  
 ACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCCAGCCAGCCGGAAGGGCCGAG  
 CGCAGAAGTGGTCTTGCAACTTTATCCGCTCCATCCAGTCTATTAATTGTTGCCGGA  
 AGCTAGAGTAAGTAGTTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG  
 GCATCGTGGTGTACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGA  
 TCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCC  
 TCCGATCGTTGTCAGAAGTAAGTTGGCCGAGTGTTATCACTCATGGTTATGGCAGCAC  
 TGCATAATTCTCTTACTGTCTATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC  
 TCAACCAAGTCATTCTGAGAAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC  
 AACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTTGGAAAAC  
 GTTCTTCGGGGCGAAAACCTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTTCGATGTAA  
 CCCACTCGTGACCCAACTGATCTTCAGCATCTTTTACTTTTACCAGCGTTTCTGGGTG  
 AGCAAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTT  
 GAATACTCATACTCTTCTTTTCAATATTTATGAAGCATTTATCAGGGTTATTGTCTC  
 ATGACATTAACCTATAAAAAATAGGCGT

FIG. 11C-2





[illegible]

TCGCCGCTTACCGGATACCTGTCCGCCCTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCAGCTGTAGGTATCTC  
 AGTTCGGTGTAAGTTCGCTCCAAAGCTGGGCTGTGTGCACGAACCCCGGTTTCAGCCCGACCGCTGCGCCTTATATCCGG  
 TAACATATCGTCTTGAGTCCAAACCCGGTAAGACACAGCACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAG  
 CGAGGTATGTAGCGGGTGTACAGAGTCTTGAAGTGGTGCCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATC  
 TCGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAAACAACCCAGCTGGTAGCGG  
 TGGTTTTTTTGTGCAAGCAGCAGATTACCGCGCAGAAAAAAGGATCTCAAGAAAGATCCTTTGATCTTTTCTACGGGGT  
 CTGACGCTCAGTGGAACGAAAACTCAGTTAAGGATTTTGGTCAATGAGATTATCAAAAAAGATCTTCAACCTAGATCCTT  
 TTAAAAATTAAAAATGAAGTTTGGCAAAATCAATCTAAAGTATATATGAGTAAACTTTGGTCTGCACAGTTACCAATGCTTAAT  
 CAGTGAGGCACCTATCTCAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCCTGACTCCCGCTCGTGTAGATAACTACGA  
 TACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTATATCAGCA  
 ATAAACCAAGCCAGCCGGAAGGCCGAGCGCAGAAAGTGTCCTGCAACTTTATCCGCCCTCCATCCAGTCTATTAAATTGTTG  
 CCGGGAAGCTAGAGTAGTTCCGCCAGTTAATAGTTTGGCAACGTTGTGCCATTGCTACAGGCATCGTGGTGTCCAC  
 GCTCGTCTGTTGGTATGGCTTTCATTACGCTCCGGTCCCAACGATCAAGCGAGTTACATGATCCCCCATGTTGTGCAAA  
 AAAGCGGTTAGCTCCTTCGGTCCCTCCGATCGTTGTGCAGAAAGTAAGTTGGCCGCGAGTGTATCACTCATGTTATGGCAGC  
 ACTGCATAATTCTCTTACTGTCTATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtagtcaaccaagtcattcttgag  
 aatagtgtagtgcggcgacccgagttgctcttgccccggcggtcaacacaggggataataccggcgccacatagcagaaactttaaaaa  
 gtgctcatcatctggaaaaacgttcttcggggcgaaaaactctcaaggatcttaccgctgtctgagatccagttcgbatgtaaac  
 cactcgtgcaccccaactgatcttcagcatcttctactcttcaaccagcgttctctgggtgagcaaaaaacaggaaggaagcaaatg  
 ccgcaaaaaaagggaaataaagggcgacacgggaaatgttgaaatactcatactcttctcttcaaatatctctgaaagcatcttat  
 cagggcttatctgtctccatgacattcaacctataaaaaatagggct

FIG.-12D







[illegible]

FIG.-13C

GCTACAGAGTTCTTGAAAGTGGTGGCCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCC  
AGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAACAACACCGCTGGTAGCGGTGTTTTTTGTGTTGCA  
AGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAC  
GAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAATAATGAAG  
TTTGGCGAAAATCAATCTAAAGTATATATAGATAAATCTGGTCTGACAGTTACCAATGCCTTAATCAGTGAGGCACCTATCT  
CAGCGATCTGTCTATTTTCGTTTCATCCATAGTTGCCCTGACTCCCCGTCGTGTAGATAAATACTACGATACGGGAGGGCTTACCA  
TCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTATATCAGCAATAAACAGCCAGCCGG  
AAGGCCGAGCGCAGAAAGTGGTCCCTGCAACTTTATCCGCCCTCCAGTCTATTAAATTGTTGCCGGGAAGCTAGAGTAA  
GTAGTTCGCCAGTTAATAGTTTGGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTACGCTCGTCTTTGGTATG  
GCTTCATTCAGCTCCGGTCCCCAACGATCAAGCGGAGTTACATGATCCCCCATGTTGTGCAAAAAGCGGTTAGCTCCTT  
CGGTCCCTCCGATCGTTGTCAGAAAGTAAAGTTGGCCGCGAGTGTATCACTCATGGTTATGGCAGCAGCTGCATAATTCTCTTA  
CTGTCAATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcatctgagaatagtgatgaggcga  
ccgagttgctcttgcccggtcaacacgggataataccgcgccacatagcagaaactttaaaagtgtcatcatgggaaa  
acgttcttcggggcaaaactctcaaggatcttaccgctgttgagatccagttcgatgtaaaccactcgtgcacccaact  
gatcttcagcatcttttactttcaccagcgtttctgggtgagcaaaaaacaggaaggcaaaatgccgcaaaaaagggaata  
agggcgacacggaaatgttgaatactactactcttccttttcaatatatttgaagcatttatcagggttattgtctcat  
gacattaacctataaaaataggcgt

FIG.\_ 13D

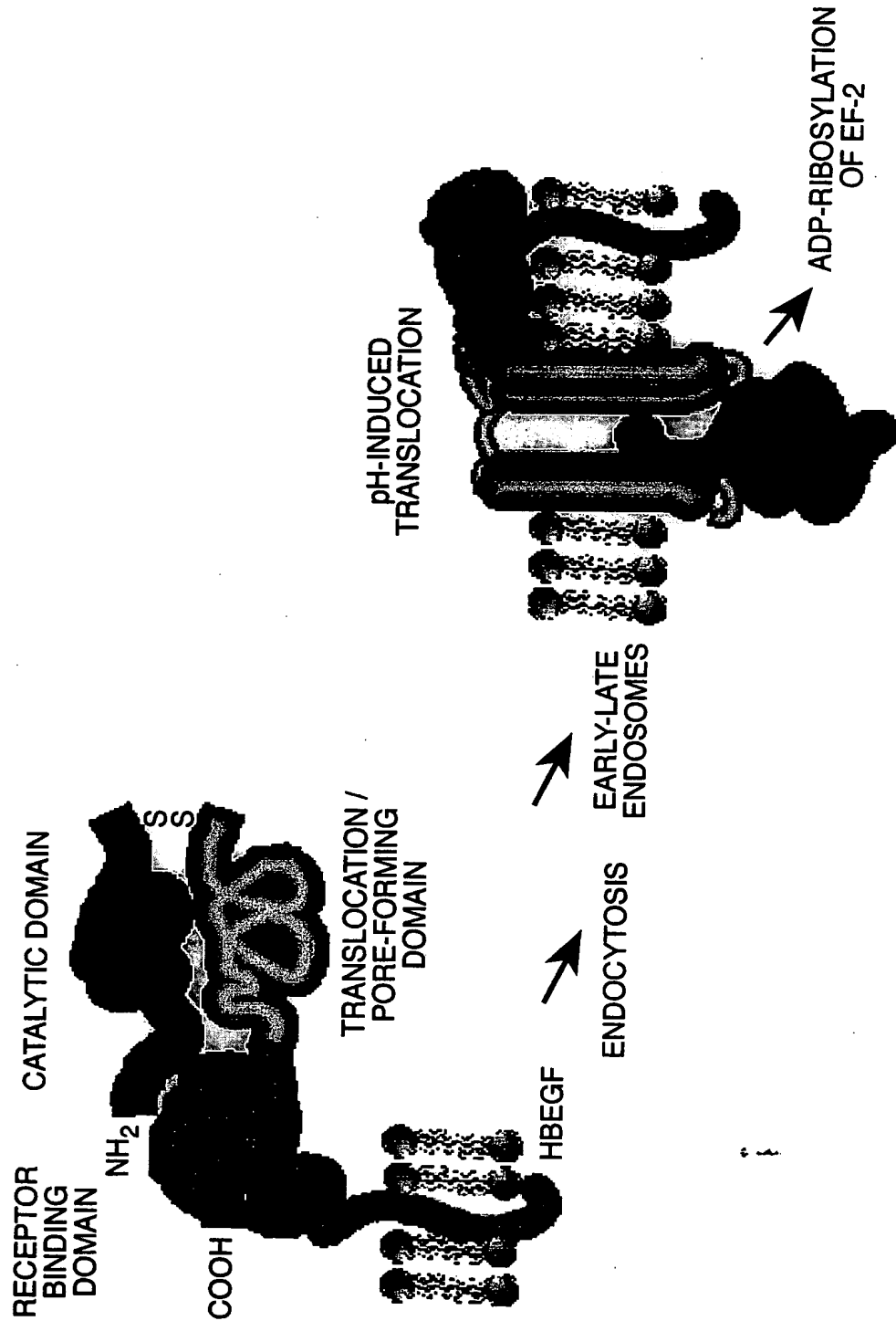


FIG.\_14

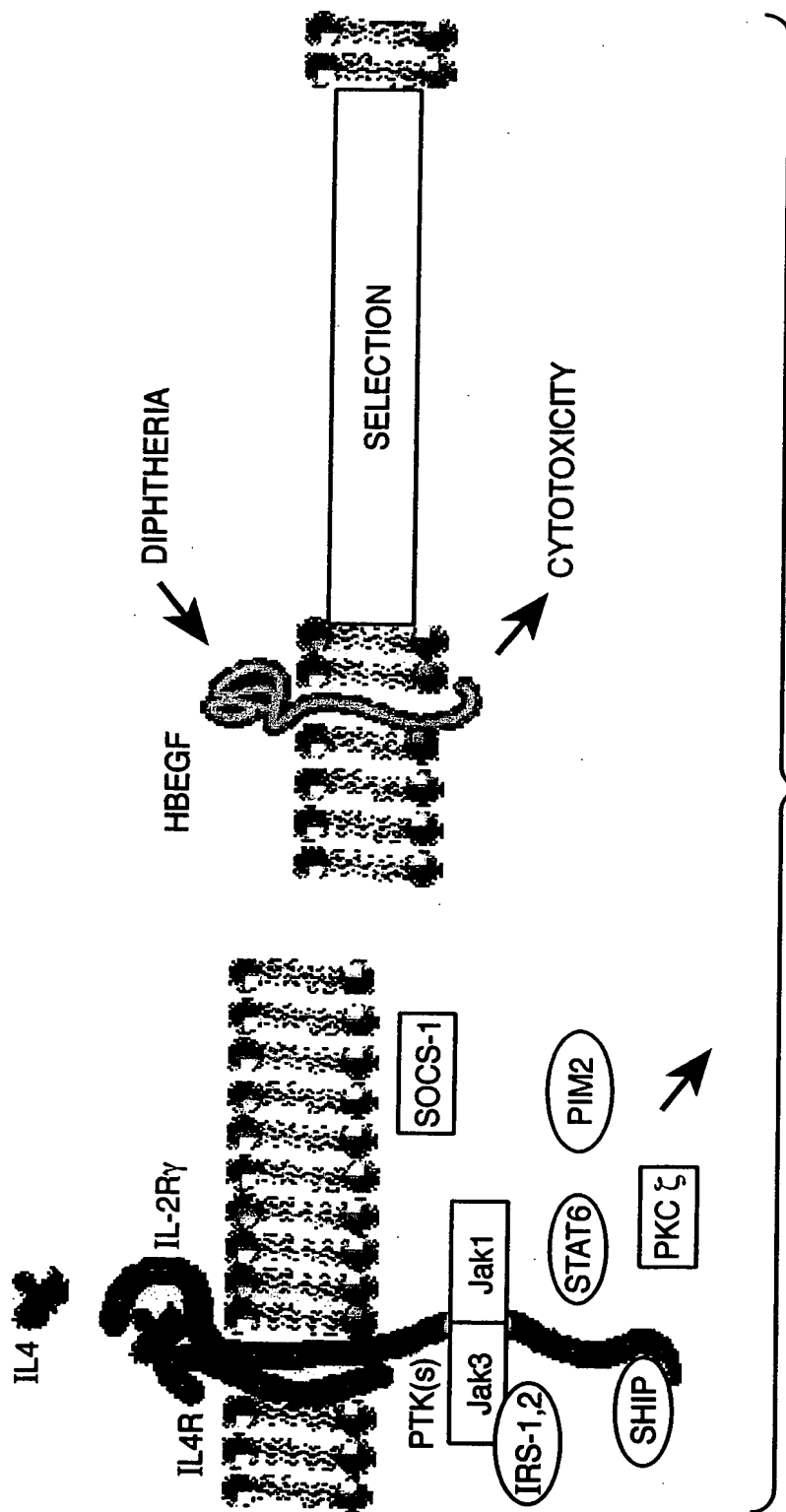


FIG. 15A

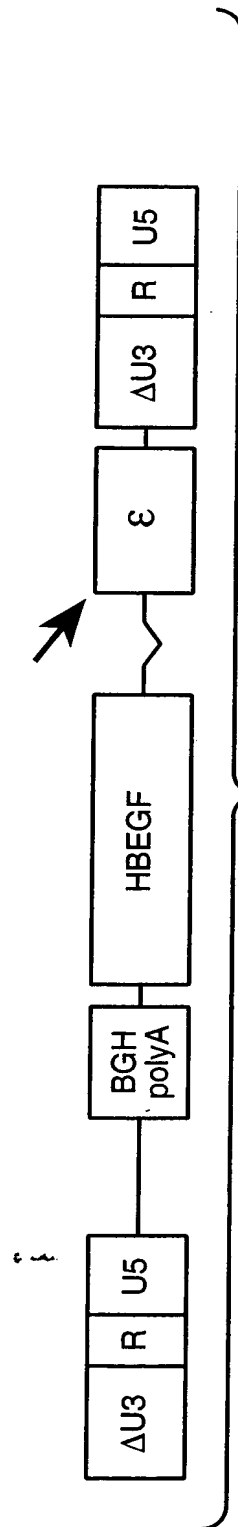
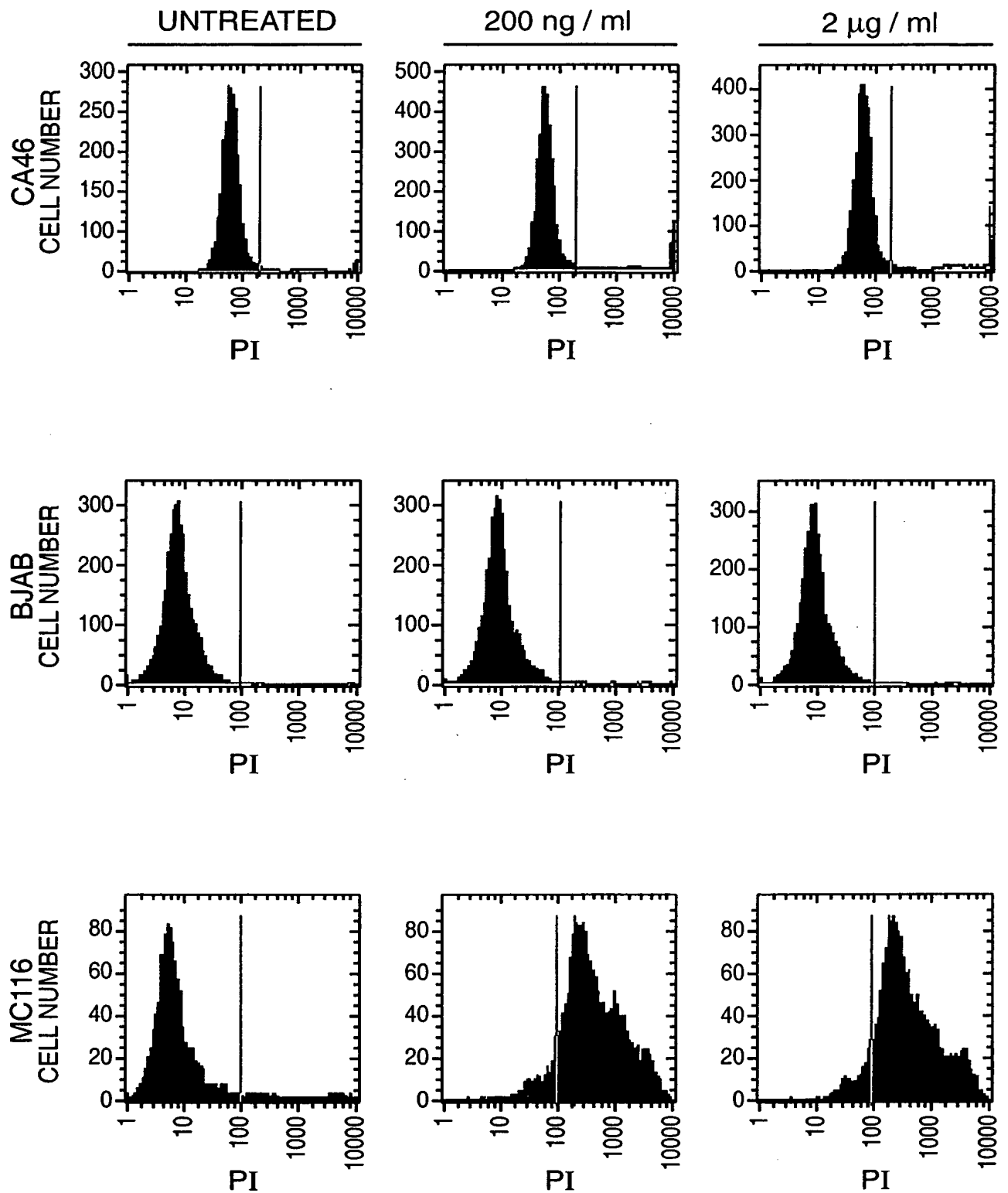
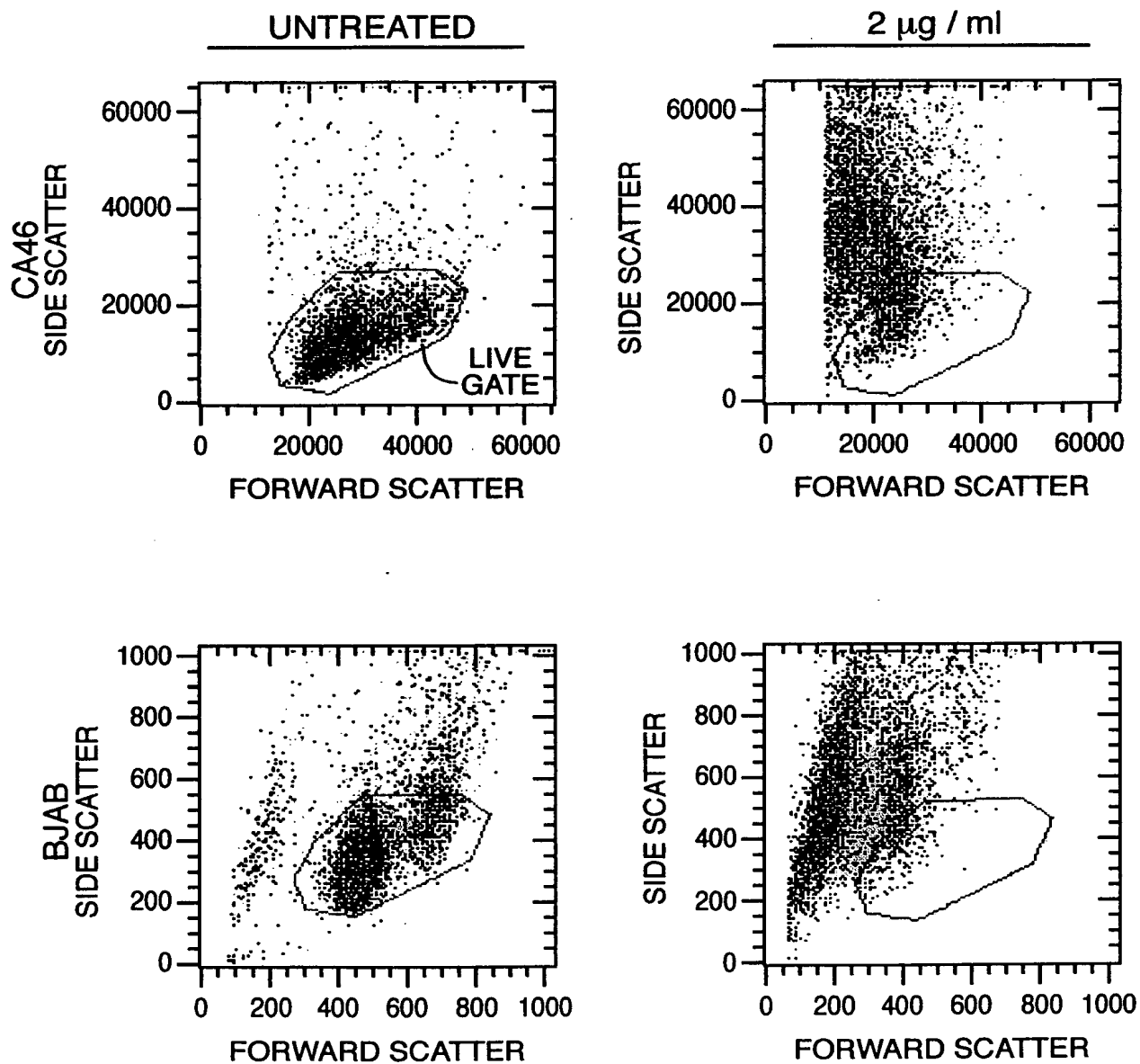
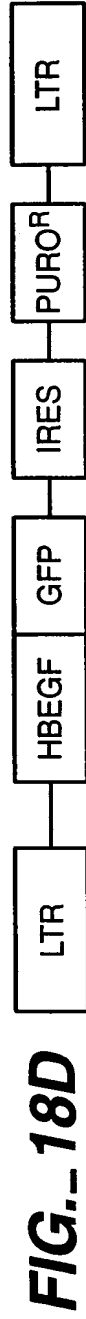


FIG. 15B

**FIG. 16**



**FIG. 17**





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